Volume 5, issue 1, 2016 • e-ISSN: 1857-8187 • p-ISSN: 1857-8179

Review Article

Trends in Mortality in Children Hospitalized with Meningococcal Infections in Albania from 2006 to 2014

Healthcare

Keywords: Meningococcal disease, meningococcemia, meningitis, children, scoring system.

Gjovalin Valca		**Faculty of Medicine, Pediatric Intensive Care, UHC "Mother Tereza", Tirana, Albania.**
Ermira Kola		**Faculty of Medicine, Pediatric Intensive Care, UHC "Mother Tereza", Tirana, Albania.**
Alketa Qosja (Hoxha)		**University of Medicine, Service of Neonatology Intensive Care Unit. Tirana, Albania.**
Ilirjana Bakalli		**Service of Pediatric Intensive Care Unit, UHC "Mother Theresa", Tirana, Albania.**
Robert Lluka		**Service of Pediatric Intensive Care Unit, UHC "Mother Theresa", Tirana, Albania.**
Durim Sala		**Service of Pediatric Intensive Care Unit, UHC "Mother Theresa", Tirana, Albania.**
Inva Gjeta		**Service of Pediatric Intensive Care Unit, UHC "Mother Theresa", Tirana, Albania.**
Ermela Gjyzeli		**Service of Pediatric Intensive Care Unit, UHC "Mother Theresa", Tirana, Albania.**
Sashenka Sallabanda		**Faculty of Medicine, Pediatric Intensive Care, UHC "Mother Tereza", Tirana, Albania.**

Abstract

Background: Lack of vaccination and modern health care facilities in many countries including Albania let meningococcemia to remain as a serious challenging disorder especially among children and in spite of improved diagnosis and earlier treatment its prognosis is still dismal. Patients expected to develop life-threatening complications in acute meningococcal infections require early recognition and appropriate monitoring. Different prognostic scoring systems have been developed. Aim: The aim of this study was to evaluate mortality in children hospitalized with meningococcal infections in Albania, including scoring systems in prognosticating mortality rate. Materials and Methods: This was a retrospective descriptive study, performed on 40 patients with definite diagnosis of meningococcal infection admitted to PICU in UHC "Mother Teresa", Tirana, Albania, between 2006 and 2014. There were 40 patients, 22(55%) males and 18(45%) females, from 2 months to 10 years old. We evaluated all the patients based on Stiehm and Damrosch and Glasgow meningococcal septicemia prognostic score. Data were collected by filling checklists. SSPS software was applied to analyze the data using chi-square test. Results: Overall mortality was 42%. According to the GMSPS(3) prognostic score of meningococcemia: 28 (70%) patients had a score <8 points and was recorded four deaths representing a mortality rate of 14.2%; the mortality rate among 12(45%) patients with a score ≥8 points resulted in 100% mortality. The sensitivity was 100%, specificity was 100%, the positive predictive value was 100% and the negative predictive value was 100% for a GMSPS score ≥8. According to the Stiehm and Damrosch criteria (2): 22(55%) patients had two or less factors present and was recorded three deaths representing a mortality rate of 13.6%; the mortality rate among 18(45%) patients with three or more factors present the mortality rate was 72.2%. The sensitivity was 90%, specificity was 80%, the positive predictive value was 75% and negative predictive value was 92.3% for the criterion ≥3 of the Stiehm and Damrosch criteria. Conclusions: Meningococci are still killers, they affect men more than women. The Stiehm and Damrosch and Glasgow meningococcal septicemia prognostic score can rapidly identify children with fulminant meningococcal disease and poor prognosis and help us starting prompt administration of suitable antibiotics, critical care and special therapeutic measures.

Introduction

Meningococcal disease (MCD) is caused by a bacterial microorganism called Neisseria meningitidis, a member of the genus Neisseria, which is an obligate human-specific pathogen that preferentially colonizes the mucous membrane of the nasopharynx[1]. Rates of meningococcal disease in the US have remained relatively stable, at approximately 0.9 to 1.5 cases per 100, 000 persons per year, or 2500 to 3000 cases per year. Meningococcemia is a medical emergency, early recognition is essential so that appropriate antibiotic therapy and supportive care can be promptly instituted[1,2]. Childhood Meningitis continues to be an important cause of mortality in many countries. Lack of vaccination and modern health care facilities in many countries including Albania let meningococcemia to remain as a serious challenging disorder especially among children and in spite of improved diagnosis and earlier treatment its prognosis is still dismal[3,4].

Meningococcal infection is a communicable disease, which is spread via pharyngeal secretion through respiratory route. Acute meningococcemia generally follows an upper respiratory infection, whereby rapid clinical deterioration may occur[5]. Meningococcal Septicemia (Meningococcemia) results from the systemic

release of various mediators in response to bacteria endotoxins leading to generalized increase in capillary permeability. Meningococcemia is characterized by shock and disseminated intravascular coagulation (DIC). Meningococcal septicemia is a fulminant infection (sometimes < 24 hours) with initial symptoms that are nonspecific (fever, muscle aches) and is difficult to diagnose before the onset of a maculopapular, petechial, or purpuric rash. Septicemia can result in rapid onset of hypotension, multiorgan dysfunction shock, peripheral ischemia, limb loss, and death. Meningococcal Meningitis is the invasion of the meninges and crossing of the blood-brain barrier with the sequential liberation of endotoxins and activation of pro- and anti-inflammatory cytokines are the underlying pathophysiological processes of the clinical picture from meningococcal meningitis. Overall mortality for invasive meningococcal disease is approximately 10% of infected individuals but is up to 40% in cases of septicemia[6,7,8]. In clinical practice, meningitis and sepsis, or more often a combination of both, are the most commonly encountered conditions. The main purpose of the paediatric intensive care unit (PICU) is to prevent mortality by intensively monitoring and treating critically ill children who are considered at high risk of mortality. Since 1966, 25 specific scoring systems have been proposed to identify the degree of severity of meningococcal diseases. More than 12 prognostic scores have been developed to predict mortality[9,10,11]. Physicians are in general poor prognosticators[12,13]. To meet the need for a rapid clinically based assessment, several prognostic scoring systems have been devised, the most popular of which are Stiehm and Damrosch and Glasgow meningococcal septicemia prognostic score (GMSPS)[3,4]. The importance of early recognition of meningococcemia through clinical, laboratory findings and prognostic score continues to be a major concern for clinicians and especially for us.

Materials and Methods

Design: Retrospective case-note study.

Setting: Pediatric Intensive Care Unit in UHC "Mother Teresa", Tirana, Albania.

Patients: Forty children with proven meningococcal septicemia (some with concurrent meningitis) from January 1, 2006 to December 31, 2014. We evaluated all the patients based on Stiehm and Damrosch criteria (Table.2) and Glasgow meningococcal septicemia prognostic spore (Table.3).

Table 2. Stiehm and Damrosch criteria[2]

1. Petechiae present for less than 12 hours before admission
2. Hypotension (systolic blood pressure< 70mm Hg)
3. Absence of meningitis (<20 WBCs in CSF)
4. Peripheral white blood cell count<10,000/mm3
5. ESR < 10 mm/hour

Table 3. (GMSPS) Glasgow Meningococcal Septicemia Prognostic Score[3]

Criteria	Score
Hypotension*	3
Skin/rectal temperature differences>3°C	3
Base deficit (capillary sample) <8mmol/l	1
Coma score**<8 at any time or deterioration of 3 ≥ in an hour	3
Lack of meningitis	2
Parental opinion that child's condition has become worse over the past hour	2
Widespread ecchymoses or extending lesions on review	1

*Systolic BP<75mm if below4 years of age, <85 if older

** Modified pediatric coma scale. (Simpson and Reilly)

We presumed a score over 8 out of 15(GMSPS) and three or more factors out of Stiehm and Damrosch systems as fatal outcome. All patients received the same therapy on admission.

Statistical Analysis

Data analysis was conducted using SPSS 18 statistical software (SPSS Inc., Chicago, IL, USA). We compared clinical characteristics on admission between patients with meningococcemia who died and those who survived. We used ROC curves to analyze sensitivity and the specificity and to highlight the positive and predictive value of our variables.Statistical significance was set at a =0.05. All statistical tests were two tailed.

Results

The age distribution of patients was as follows: 7(17.5%) < 1 year old, 27 (67.5%), 1-5 years, 6(15%), 6-10 years old (Tab.1 and Fig. 1).

Figure 1. Frequency of age.

Age	N	%
<1 year old	7	17.5%
1-5 years old	27	67.5%
>5-10 years old	6	15%

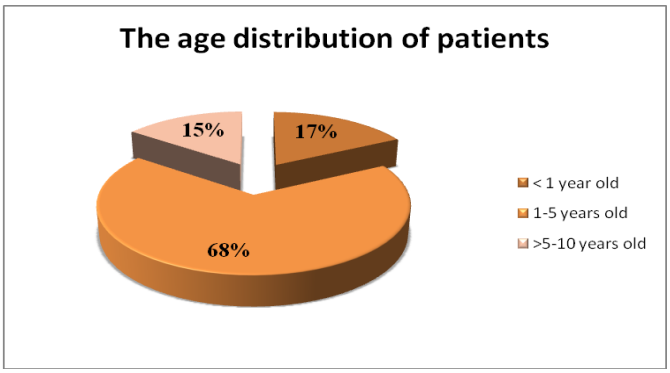


Table 1. Frequency of age

The season prevalence declined in the order of winter 5(12.5%), spring 13(32.5%), summer 7(17.5%) and fall 15(37.5%), (Tab.2 and Fig. 2).

Figure 2. The season prevalence of meningococcemia

Seasons	N	%
Winter	5	12.5%
Spring	13	32.5%
Summer	7	17.5%
Fall	15	37.5%

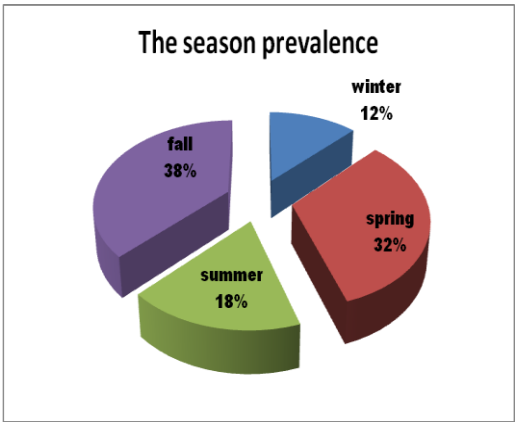


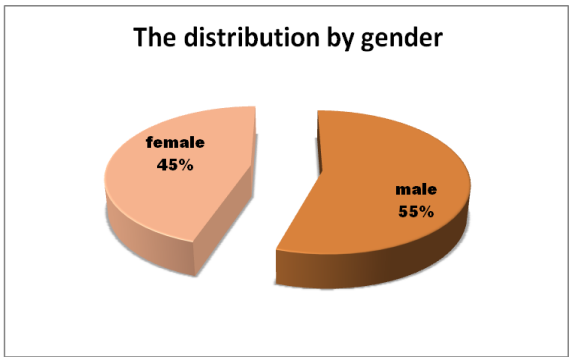
Table 2. The season prevalence of meningococcemia

We found a distribution of the disease by gender in the following report: Female 18 (45 %) and male 22 (55 %), there is a preponderance of men who are more risked (Tab. 3 and Fig. 3).

Gender	N	%
Male	22	55%
Female	18	45%

Table 3. The distribution by gender

Figure 3. The distribution by gender



Stiehm and Damrosch criteria	Number of patients (n,%)	Deaths (n,%)
Petechiae present for less than 12 hours before admission	27 67.5%	12 44.4%
Hypotension (systolic blood pressure< 70mm Hg)	18 45%	16 88.8%
Absence of meningitis (<20 WBCs in CSF)	18 45%	13 72.2%
Peripheral white blood cell count<10,000/mm3	24 60%	15 62.5%
ESR < 10 mm/hour	11 27.5%	8 72.7%

Table 4. Distribution of patients according to Stiehm and Damrosch criteria

Glasgow Meningococcal Septicemia Prognostic Score	**Number of patients (*n,%*)**	**Deaths (*n,%*)**
Hypotension	18 *45%*	16 *88.8%*
Skin/rectal temperature differences>3°C	16 *40%*	16 *100%*
Base deficit (capillary sample) <8mmol/l	16 *40%*	16 *100%*
Coma score<8 at any time or deterioration of 3 ≥ in an hour	16 *40%*	16 *100%*
Lack of meningitis	18 *45%*	13 *72.2%*
Parental opinion that child's condition has become worse over the past hour	24 *60%*	16 *66.6%*
Widespread ecchymoses or extending lesions on review	27 *67.5%*	12 *44.4%*

Table 5. Distribution of patients according to Glasgow Meningococcal Septicemia Prognostic Score

Sixteen deaths were recorded, representing an overall mortality rate of 42%. None of the patients had received meningococcal vaccination. According to the GMSPS(4) prognostic score of meningococcemia: 28 (70%) patients had a score <8 points and was recorded four deaths representing a mortality rate of 14.2%; the mortality rate among 12(45%) patients with a score ≥8 points resulted in 100% mortality. The sensitivity was 100%, specificity was 100%, the positive predictive value was 100% and the negative predictive value was 100% for a GMSPS score ≥8.

According to the Stiehm and Damrosch criteria (2): 22(55%) patients had two or less factors present and was recorded three deaths representing a mortality rate of 13.6%; the mortality rate among 18(45%) patients with three or more factors present the mortality rate was 72.2%. The sensitivity was 90%, specificity was 80%, the positive predictive value was 75% and negative predictive value was 92.3% for the criterion ≥3 of the Stiehm and Damrosch criteria.

Discussion

Numerous studies have looked at factors predictive of poor outcome in meningococcal disease, since the seminal study of Stiehm and Damrosch in 1966, which identified petechiae, hypotension, absence of meningitis, peripheral leukopenia and low erythrocyte sedimentation rate (ESR) as markers of a poor prognosis[15].

During the study period 2006-2014 there were 40 patients from 2 months to 10 years old. The most frequent age group was 1-5 years (67.5%), differently from other countries, where the incidence of invasive meningococcal disease in pediatric patients has two peaks: the first peak with the highest incidence in infants younger than 12 months, the second peak in adolescents[16]. The ratio male/female was 1.3 similar to data in the literature[17, 18].

The incidence, according to the Public Health Department, has been low, with an average of 0.24/100000 inhabitants, as it is in countires of low incidence, while the majority of meningococcal disease in Europian countires range in incidence from 0.2-14 cases per 100000 inhabitants[19]. Even though the incidence was low, the mortality rate in our country remaind high ~ 42%, with most deaths occurring within 48 hours of admission. Many academic medical centers report overall mortality rates of 5-10% [20].

In our study we found that, the absence of meningitis, shock and Glasgow Coma Scale ≥8 points as significant predictors for death. According Algreen et al. [21] the absence of meningeal involvement was not a good predictors of mortality, and that a low white count, the presence of a rash and altered mental status, particulary coma, were sensitivity indicators of mortality. Even in our study, significant laboratory findings to predict mortality were total white blood count < 10000mm^3 in 62.5% of cases, skin/rectal temperature differences>3°C in 100% of cases, severe basis deficit in 100% of cases and low ESR. Similar data are reported in the literature [22].

GMSPS and the Stiehm and Damrosch criteria which combine clinical and laboratory markers continue to have clinical utility [20].

In our study, the sensitivity was 100%, specificity was 100%, the positive predictive value was 100% and negative predictive value was 100% for GMSPS score>5, thus confirming the positive predictive value, the negative predictive value and the high sensitivity of this scoring system. For the Stiehm and Damrosch criteria >2 we found that the sensitivity was 90%, specifity was 80%, positive predictive value was 75% and negative

predictive value was 92.3%, meaning that this scoring system is accurate in identifying patients with good outcome, as good as predicting poor outcome.

Regarding this severe presentation in our country, we lack data about the serotype of meningococcal. Given that from our results, none of the patients had a history of meningococcal vaccination, we believe that identifying the unfavorable prognostic factors helps to decrease the mortality rate, but the best way is preventing infection through meningococcal vaccination, which raises the need for meningococcal vaccination in our country.

Conclusions

The GMSPS is a rapid clinical score that performs well in identifying children with poor prognosis and is an easily performed, repeatable, clinical score that can rapidly identify children with fulminant meningococcal disease. We recommend that every physician who treats patients with meningococcemia must consider the prognostic alarms, GMSPS score system.

Conflict of Interest Statement

No conflict of interest was declared. This article was not sponsored by any external organization.

References

1. Mark B. Salzman, Lorry G. Rubin. Infectious Disease Emergencies: Infectious Disease Clinics of North America. 1996; 10: 709-72.
2. Gedde-Dahl TW, Bjarke P, Høiby EA, Host JH, Bruun JN. Severity of Meningococcal disease: assessmentby factors and scores and implications for patient management. Rev Infect Dis. 1990; (6):973-92.
3. Richard Stiehm E, Douglas S Damrosch. Factors in the prognosis of meningococcal infection .Medical progress.1966; 68:457-467.
4. Riordan FA, Marzouk O, Thomson AP, Sills JA, Hart CA). Prospective validation of the Glasgow Meningococcal Septicaemia Prognostic Score. Comparison with other scoring methods. Eur J Pediatr. 2002 Oct;161(10):531-7.
5. Simpson D, Reilly P. Pediatric coma scale. Lancet.1985; ii: 450.
6. Bruce MG, Rosenstein NE,Capparella JM. Risk factors for meningococcal disease in college students. JAMA 2001;286 : 688-693.
7. Goldacre MJ, Roberts SE, Yeates D. Case fatality rates for meningococcal disease in an English population, 1963–1998: database study. BMJ. 2003; 327(7415):596–597.
8. Qiuzhi Chang, Yih-Ling Tzeng, David S Stephens. Meningococcal disease: changes in epidemiology and prevention. Clinical Epidemiology 2012: 4, 237–245.
9. Lisa A. Jackson, M.D. Jay D. Wenger, M.D. Laboratory-Based Surveillance for Meningococcal Disease in Selected Areas, United States, 1989-1991. MMWR CDC Surveill Summ. 1993 Jun 4;42(2):21-30.
10. Leteurtre S, Leclerc F, Martinot A, et al: Can generic scores (Pediatric Risk of Mortality and Pediatric Index of Mortality) replace specific scores in predicting the outcome of presumed meningococcal septic shock in children? Crit Care Med 2001, 29:1239–1246
11. Health Protection Agency Meningococcus Forum. Guidance for public health management of meningococcal disease in the UK. London: Health Protection Agency; 2006.
12. Ragunathan L, Ramsay M, Borrow R, Guiver M, Gray S, Kaczmarski EB. Clinical features, laboratory findings and management of meningococcal meningitis in England and Wales: report of a 1997 survey. Meningococcal meningitis: 1997 survey report. J Infect 2000;40(1):74-9.

13. Rosana Carla de Freitas Aragão, Maria de Fátima P. Risk Factors Associated with Death in Children Admitted to a Paediatric Intensive Care Unit. J Trop Pediatr (2001) 47 (2): 86-91.
14. Poonam Bhadoria, Amit G Bhagwat. Severity Scoring Systems in Paediatric Intensive Care Units, Indian Journal of Anaesthesia 2008;52:Suppl (5):663-675.
15. Stiehm ER, Damrosch DS. Factors in the prognosis of meningococcal infection. Review of 63 cases with emphasis on recognition and management of the severely ill patient. J Pediatr. 1966;68:457–467)
16. American Academy of Pediatrics Committee on Infectious Diseases. Prevention and control of meningococcal disease: recommendations for use of meningococcal vaccines in pediatric patients. Pediatrics. 2005; 116(2):496-505.
17. Naeni E. Importance of scoring systems in prognosticating meningococcemia. Journal of research in Medical Sciences. 2005; 1: 34-7.
18. Mamishi S, Mostashfi S. Clinical and laboratory manifestation of meningococcemia in children. Iranian J Publ Health. 2006; 35(4): 49-53.
19. Harrison LH, Trotter CL, Ramsay ME. Global epidemiologyof meningococcal disease. Vaccine. 2009; 27 (2): 51-63.
20. Castellanos-Ortega A, Delgado-Rodrigues M, et al. A new prognostic scoring system for meningococcal septic shock in children. Comparison with three other scoring systems. Intensive Care Med. 2002; 28 (3): 341-51.
21. Algren JT, Suresh L, et al. Predictors of outcome in acute meningococcal infection in children. Crit Care Med. 1993; 21 (3): 447-52.
22. Duarte MC, Amorim MR, Cuevas LE. Risk factors for death from meningococcal infection in Recife, Brasil. J Trop Pediatr. 2005; 51(4): 227-31.